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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,301	10/24/2003	Gary K. Schwartz	702-A-US	1477

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EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/693,301	SCHWARTZ, GARY K.	
	Examiner	Art Unit	
	Paul C. Martin	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-38, 41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-38,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2003 and 15 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/15/03& 05/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 31-38, 41 and 42 are pending in this application.

Election/Restrictions

Applicant's response to the restriction requirement, filed on 09/29/05 is acknowledged. The Examiner acknowledges overlooking the Preliminary Amendment filed on 10/24/03 and therefore removes the previous restriction requirement.

Claims 31-38, 41 and 42 were examined on the merits.

Information Disclosure Statement

The information disclosure statement filed 12/15/03 fails in part to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the cited references #6 and #8 were not included. It has been placed in the application file, but the references in #6 and #8 referred to therein have not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Drawings

Figure 1 should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The informal drawings labeled Figs. 6, 10, 13 and 14 are not of sufficient quality to permit examination. Accordingly, replacement drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to this Office action. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action.

Applicant is given a TWO MONTH time period to submit new drawings in compliance with 37 CFR 1.81. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a). Failure to timely submit replacement drawing sheets will result in ABANDONMENT of the application.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

Replacement Drawing Sheets

Drawing changes must be made by presenting replacement sheets which incorporate the desired changes and which comply with 37 CFR 1.84. An explanation of the changes made must be presented either in the drawing amendments section, or remarks, section of the amendment paper. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). A replacement sheet must include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of the amended drawing(s) must not be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and within the top margin.

Annotated Drawing Sheets

A marked-up copy of any amended drawing figure, including annotations indicating the changes made, may be submitted or required by the examiner. The annotated drawing sheet(s) must be clearly labeled as "Annotated Sheet" and must be presented in the amendment or remarks section that explains the change(s) to the drawings.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability.

Specification

The use of the trademark Taxol™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 41 and 42 are objected to because of the following informalities: Presence of trademark Taxol™ in claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for aqueous extraction of *Coptis chinesis*, does not reasonably provide enablement for all the possible methods of extraction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. There is no guidance or direction presented to direct one to determine which substances would work in the broadly claimed invention, which is a complex and unpredictable art. Therefore because of the large number of potential embodiments claimed, the ordinary artisan would be subjected to undue experimentation to practice the claimed invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The state of the art is unpredictable with regard to plant extracts. Applicants teach an aqueous extraction method for preparing their *Coptis chinesis* and reference the methods of alcohol and mineral oil extraction, with or without heating. Applicant has not demonstrated, and it is highly questionable that only these specific extraction methods are suitable for the satisfactory extraction of *Coptis chinesis*.

It is well known in the art that polarity of solvents plays a key role in determining the final product obtained by an extraction. However, because many phyto-chemicals remain undiscovered, the skilled artisan has to make his best educated guess as to what types of phyto-chemicals will be successfully extracted with a solvent of a particular polarity. Often times, unless the constituents in a particular plant extract have been well evaluated and documented in the literature, the skilled artisan must adhere to trial and error protocols in order to quantitatively determine phyto-chemical constituents present in samples obtained from respective extraction procedures. These procedures are common when, for example, a plant or part thereof has been documented in the literature as possessing some medicinal quality. The skilled artisan will attempt numerous extraction protocols in attempt to isolate the particular ingredient which has this medicinal quality. Typically, beginning with the first crude extraction, it is a guess as to whether or not the extract will possess certain phyto-chemical constituents. It is noted that the Instant specification does disclose several of the active ingredients of the extract; though only teaches certain extracts which provide for the effective ingredient *berberine*.

Each successive extraction of plant matter yields different products due to the exclusion of ingredients based on the polarity of the solvents solvating constituents with similar polarities. Subsequently, the properties of each respective product are unpredictable and would need to be evaluated for chemical constituents.

Unpredictability with regard to plant extracts due to their highly complex nature has been well documented in the art. Revilla et al. for example (1998) showed that the ***slightest variations in polarity of solvent and reaction time*** upon grape extraction provided respective products with unique characteristic properties (See Tables 1, 2, 4, 5, 6 and 7). In turn, each product would possess varying pharmacological properties based upon their respective methods of extraction. Further contributing to the unpredictability of plant extracts, it has been determined that in some cases, the active agent is not a single ingredient, but a combination of ingredients working synergistically to provide a therapeutic effect:

"The blood red sap from the bark of several species of Croton (Euphorbiaceae) are used in traditional medicine in S. Amnerica to treat wounds and a series of diseases including cancer. More than 90% dry weight of the sap consists of mixtures of proanthocyanidins ranging from monomers to heptamers and even to polymers of twenty units. We have established the chemical structures of these oligomers and the monomeric units are either catechin or gallocatechin...In addition, we isolated some novel diterpenoids and a series of simple phenols as minor constituents. As a result of biological tests we have concluded that here is no single ingredient for would healing but that the whole sap contributes to the healing process" (Phillipson, J. 1999).

It is the opinion of the Examiner, in light of the grave unpredictability in the art with regard to plant extracts, that Applicant is not enabled for any extract as Instantly claimed. Each product obtained from an extraction is unpredictable in nature. Even the most skilled of artisans would need to quantify each product for constituents as well as medicinal efficacy. Considering this evidence, the skilled artisan, lacking information with regard to any other solvents which will produce the Instantly claimed phyto-chemicals, would necessarily need to perform tedious trial and error protocols without expectation of success in order to ascertain what other extracts would provide for the specific therapeutic uses as described in the specification.

The entire scope of the claims has not been enabled because:

1. Quantity of experimentation necessary would be undue because of the large number of techniques and methods claimed.

2. Amount of direction or guidance presented is insufficient to predict which methods encompassed by the claims would work.

3. Presence of working examples are only specific to aqueous extraction and alternate methods have not been specifically taught or suggested.

4. The nature of the invention (phytochemical extracts) is complex and unpredictable.

5. Level of predictability of the art is very low.

6. Breadth of the claims encompasses an innumerable number of methods and techniques.

7. The level of one of ordinary skill in this art is variable.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

Claims 34, 35, 41 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic.

In re Gostelli, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe the subgenus. *In re Gostelli*, F.2d at 1012, USPQ2d at 1618.

As stated *supra*, the MPEP states that the written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable, that Claims 34, 35, 41 and 42 are broad generics, with respect to all possible protein kinase-c inhibitors, microtubule destabilizing agents, and "taxol-like" compounds. The possible variations as disclosed in the specification are limitless, and examples reflecting the variety of possible species in the genus are not provided.

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonable convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 41 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The description "taxol-like" is indefinite and fails to point out the metes and bounds of the claims. Further, it is noted in the art at the time of invention that Taxol™ is a *microtubule stabilizing agent* (Arnal et al. 1995). It is also noted in the specification that the compound nocodazole is taught as a microtubule destabilizing agent, however nocodazole is **not** a taxol and does not have any of the functional characteristics of a taxol.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Hong-fen *et al.* (2001) as evidenced by Xu *et al.* (1994) and Das *et al.* (1995). *

Hong-fen et al. teaches the treatment of solid tumors comprising administering to rats an effective amount of *Coptis chinensis* extract (Pg. 1947, Abstract and Pg. 1948-49, Paragraphs 2.2-2.5) which further comprises a protein kinase-c inhibitor. Compounds found in ACNO such as *Curcuma zedoaria* and *Salvia miltiorrhiza* are known protein kinase-c inhibitors. (Xu *et al.* (abstract only) and Das *et al.* (Column 2, Lines 34-37)

* These references are cited merely to relay an inherent properties of *Curcuma zedoaria* and *Salvia miltiorrhiza* and are not used as a basis for rejection *per se*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-38, 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hong-Fen *et al.* (2001) in view of Xinxian, 6,290,995 and Alloatti *et al.* (1998).

Hong-fen *et al.* teaches a method for treating cancer in a subject by administering an effective amount of an extract containing *coptis chinesis*, and other therapeutic agents which are known protein kinase-c inhibitors as discussed *supra.*

Hong-fen *et al.* does not teach using a microtubule destabilizing therapeutic agent that is a taxol or "taxol-like". Nor does the reference teach any sequence of administration of the *coptis chinesis* and therapeutic agent.

Xinxian teaches that taxol is an anti-cancer drug that has the characteristic of promoting the assembly of microtubules. Xinxian notes that taxol has the associated problem of being poorly water soluble. Xinxian further teaches the use of the cancer treating extracts from two plants, one of which is high in berberine, an active component found in *coptis chinesis.* (Column 1, Lines 26-36 and Table 1)

Aloatti *et al.* teaches the use of taxol and taxol-analogs as a known anti-cancer treatment that acts to inhibit microtubule disassembly, active against a wide range of solid tumors, though with some serious clinical side effects. (Pg. 561, Column 1, Lines 1-14)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to include a microtubule "destabilizing" agent in a sequential regimen with the extract containing *coptis chinesis* and a protein kinase-c inhibitor and would have had motivation to do so because sequential treatments allow the researcher to assay efficacy, toxicity, possible side effects, or benefits of each compound separately. Further, the compounds act through different mechanisms and pathways and may work under different time frames.

It is also noted that since taxols are not readily water soluble, a second preparation would likely be needed since administration in tandem with the *coptis* extract would not be suitable.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one with ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence or evidence to the contrary.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Paul Martin
Examiner
Art Unit 1655

10/26/05

PATRICIA LEITH
PRIMARY EXAMINER